

**REMARKS**

This application is a continuation of application Serial No. 08/162,376, which is now U.S. Patent No. 6,013,431.

Applicants affirm the election of Group I claims 1-11, 34-39. All pending claims, including claims 12-33, have been cancelled. New claims 40-81 are drawn to subject matter consonant with Group I claims. Claims 40-60 have been restricted for examination purposes from Applicants' co-pending application Serial No. 08/465,322 where they were claims 76-96. Entry and consideration of claims 40-81 are respectfully requested.

The new claims find support in the specification. Claims 40 and 51 find support throughout the specification and for example at page 7, lines 7-12 and also at page 15, line 27 through page 16, line 5. Claims 61 and 72 find support throughout the specification and for example at page 18, lines 17-22. Claims 45-46 and 55-56 find support throughout the specification, and for example at page 16, lines 13-20. Claims 47 and 57 find support in the specification at, for example, page 17, line 12-19. Claims 49 and 59 find support in the specification, for example, at page 19, lines 26-30. Claim 41 finds support in the specification at, for example, page 10, lines 10-13. Claims 43 and 53 find support in the specification, for example, at page 15, lines 10-12.

No new matter has been added.

The new claims are directed to methods for determining the identity of a nucleotide of a target nucleic acid by primer extension using a mixture of either at least one deoxynucleotide and a chain terminating nucleotide analogue or at least one deoxynucleotide and more than one chain terminating nucleotide analogue.

**Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-11, 34-39 have been rejected under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Applicants have canceled claims 1-11, 34-39 and replaced them with new claims 40-60. Applicants reserve the right to prosecute these claims at a later date. Applicants respectfully submit that the new claims do particularly point out and distinctly claim the subject matter of the invention. Therefore, Applicants respectfully submit that this rejection has been obviated.

**Rejections Under 35 U.S.C. § 102(a)**

Claims 1, 3, 5, 6 and 9 have been rejected under 35 U.S.C. § 102(a) as being anticipated by Kuppuswamy et al. (BLOOD 74(7) suppl 1 November 1989, page 254a). Claims 1-11 have been rejected under 35 U.S.C. § 102(a) as being anticipated by European Patent Application EP 0 332 435 A2 “Newton et al”. Claims 1, 3, 5, 6 and 9 have been rejected under 35 U.S.C. § 102(a) as being anticipated by European Patent Application EP 0 246 864 A2 “Carr”.

With respect to Kuppuswamy et al., Applicants have canceled 1, 3, 5, 6, and 9. The new claims include either the step of “exposing the hybridized nucleic acid polymer to a polymerization agent in a mixture of at least one deoxynucleotide and a chain terminating nucleotide analogue” (claims 40 and 51) or the step of “exposing the hybridized nucleic acid polymer to a polymerization agent in a mixture of at least one deoxynucleotide and more than one chain terminating nucleotide analogue” (claims 61 and 72). These steps include the use of **a mixture of at least one deoxynucleotide and a chain terminating nucleotide analogue**. Kuppuswamy et al., however, use a labeled

deoxynucleotide corresponding to either the wild type nucleotide or the variant nucleotide. Kuppuswamy et al. does not disclose a step including the use of **a mixture of at least one deoxynucleotide and a chain terminating nucleotide analogue**.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection in light of the new claims and arguments made herein.

With respect to Newton et al., Applicants have canceled claims 1-11. The new claims include the step that “the primer binds to a nucleotide flanking the specific nucleotide at the defined site in the target nucleic acid.” In contrast, Newton et al. teach annealing the primer such that the 3' terminus of the primer includes the nucleotide of the point mutation. Newton et al. does not disclose a step that “the primer binds to a nucleotide flanking the specific nucleotide at the defined site in the target nucleic acid.” Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection in light of the new claims and arguments made herein.

With respect to Carr, Applicants have canceled 1, 3, 5, 6, and 9. The new claims include either the step of “exposing the hybridized nucleic acid polymer to a polymerization agent in a mixture of at least one deoxynucleotide and a chain terminating nucleotide analogue” (claims 40 and 51) or the step of “exposing the hybridized nucleic acid polymer to a polymerization agent in a mixture of at least one deoxynucleotide and more than one chain terminating nucleotide analogue” (claims 61 and 72). Carr, to detect a mutant, determines the efficiency of incorporation of a particular nucleotide to join two oligonucleotide probes (see Carr page 3, lines 35-37). Carr does not disclose the use of chain terminators in a step of “exposing the hybridized nucleic acid polymer to a polymerization agent in a mixture of at least one deoxynucleotide and a chain terminating nucleotide analogue”. Nor does Carr teach or suggest the step of “analyzing the polymerization mixture of step (c) for the presence or absence of the primer extension product” or “analyzing the polymerization mixture of step (c) for the primer extension

product” as in new claims 40 and 51, respectively. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection in light of the new claims and arguments made herein.

**Rejection Under 35 U.S.C. § 102(b)**

Claims 1, 3, 4, 5, 7, 8, 9 and 34 have been rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 4,656,127 issued to Mundy.

Applicants have canceled claims 1, 3, 4, 5, 7, 8, 9 and 34. Mundy discloses a method whereby mutants are detected by determining whether a modified nucleotide confers exonuclease resistance to a probe after having been linked to the probe. The present invention as claimed, by contrast, includes either the step of “analyzing the polymerization mixture of step (c) for the presence or absence of the primer extension product containing the labeling moiety at the 3' end thereof, whereby the identity of the specific nucleotide at the defined site is determined” (claims 40 and 61) or the step of “analyzing the polymerization mixture of step (c) for the primer extension product, whereby the identity of the specific nucleotide at the defined site is determined” (claims 51 and 72). Such steps are not taught or suggested by Mundy, which analyzes whether digestion of an oligonucleotide probe occurs or not depending on addition of an exonuclease resistant nucleotide. Applicants respectfully request reconsideration and withdrawal of this rejection in light of the new claims and arguments made herein.

**Rejections Under 35 U.S.C. § 102(g)**

Claims 1-5, 7-11, 34-35 and 37-39 are rejected under 35 U.S.C. § 102(f) as being anticipated by U.S. Patent No. 5,888,819 issued to Goelet et al. Claims 1, 3, 5, 6, 9, and 34-39 are rejected under 35 U.S.C. § 102(f) as being anticipated by U.S. Patent No. 5,846,710 issued to Bajaj. And claims 1-5, 7-11 and 34-39 are rejected under 35 U.S.C. § 102(f) as being anticipated by U.S. Patent No. 6,004,744 issued to Goelet et al.

Applicants will assume that the Examiner intended the above rejections under 35 U.S.C. § 102(g).

Applicants have canceled claims 1-11, 34-39. The new claims all comprise either the step of “exposing the hybridized nucleic acid polymer to a polymerization agent in a mixture of at least one deoxynucleotide and a chain terminating nucleotide analogue” (claims 40 and 51) or the step of “exposing the hybridized nucleic acid polymer to a polymerization agent in a mixture of at least one deoxynucleotide and more than one chain terminating nucleotide analogue” (claims 61 and 72). These steps include the use of **a mixture of at least one deoxynucleotide and a chain terminating nucleotide analogue**. This step has been found to patentably distinguish the invention from the methods of Goelet et al. and Bajaj. See, for example, reasons for allowance of U.S. application Serial No. 08/162,376, now U.S. Patent No. 6,013,431. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection in light of the new claims and arguments made herein.

#### **Obviousness-type Double Patenting Rejection**

Claims 1-11 and 34-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of U.S. Patent No. 6,013,431.

Applicants have canceled claims 1-11 and 34-39. Applicants, therefore, respectfully submit that this rejection has been obviated.

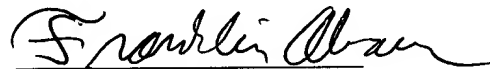
#### **Conclusion**

In view of the foregoing Amendment to the claims, and the remarks set forth above, reconsideration and allowance are respectfully solicited.

If any additional fees are determined to be necessary or any overpayment has been made, please charge or credit our Deposit Account No. 11-0171 as appropriate.

If the Examiner has any questions or suggestions of possible amendment for allowance, the Examiner is cordially invited to contact Applicants' attorney at the telephone number provided below.

Respectfully submitted,



Franklin S. Abrams  
Registration No. 43,457  
Attorney for Applicants

Kalow & Springut LLP  
Telephone: (212) 813-1600  
Facsimile: (212) 813-9600